is still an important drug for the treatment of staphylococcal infections, the detection of any mechanism conferring resistance to this drug may be important for predicting the clinical outcome.

Our findings confirm that the reliable detection of MLS resistance conferred by inducible $N^6$-dimethylase activity in staphylococci by disk diffusion requires the apposition of the lincosamide next to the erythromycin disk; the substitution of lincomycin for clindamycin further increases the sensitivity of the resistance screening.

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## Nasopharyngeal carriage of *Streptococcus pneumoniae* in children's day-care centers: 10-month follow-up study in Nice, France

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*Streptococcus pneumoniae* (SP) is one of the most frequently encountered bacterial species in respiratory tract infections, occasionally leading to potentially life-threatening complications (meningitis, septicemia). Since 1987, a steady increase in resistance has been observed in France, with rates reaching 32% in 1994 [1]. Every child carries SP at some time during the year and this organism is responsible for the majority of bacterial infections between 3 months and 3 years of age [2]. However, epidemic processes within day-care centers do not appear to have been investigated to date. The object of this study was to assess the prevalence and incidence of nasopharyngeal carriage of penicillin-resistant pneumococci (PRP), and identify risk factors associated with carriage in a cohort of children attending day-care centers in south-eastern France.

A prospective longitudinal study was conducted between September 1994 and June 1995 in three day-care centers in the town of Nice, France. Two of these were hospital day-care centers catering for children of hospital staff (DCCs A and P), while the third was a private center (DCC S). A nasopharyngeal sample was collected monthly, starting at inclusion and for as long as the child attended the center. Care-givers and parents were interviewed each time to investigate recent upper or lower respiratory tract infections and/or antimicrobial treatment. Samples were collected with a flexible Vygon 522.06 tube fitted onto a 1-mL syringe and introduced into one of the child's nostrils. SP strains were tested for susceptibility to oxacillin by the Kirby–Bauer method. Susceptibility to penicillin was

defined as a penicillin MIC <0.1 mg/L [3]. Resistance was defined as a penicillin MIC ≥2 mg/L; only such fully resistant isolates are considered in the epidemiologic investigation. A nested case-control study was conducted within the cohort in order to identify risk factors for PRP carriage independently of horizontal contamination among the children. Among the 28 children who acquired a PRP strain, 18 could be matched according to DCC, age, group attendance and length of stay within the DCC to 36 controls.

Over the 10-month study period, 137 children were included. In both hospital DCCs, fewer children aged over 24 months participated. Seven hundred and sixty-eight samples were collected, i.e. 5.6 samples per child (range: 1–11). Among the 768 samples, 336 (44%) contained an SP strain; 58% of these strains were susceptible to penicillin, 26% were penicillin resistant and 16% had intermediate susceptibility. Serotype 23F strains were resistant in 81% of cases and intermediately susceptible to β-lactams in 10% of cases, serotype 6 strains were susceptible in 68% of cases and never found to be resistant, and serotypes 14 and 19 were susceptible in 92% and 98% of cases, respectively.

At initial sampling, 20 children (15%) harbored a PRP (MIC ≥2 mg/L) strain. Among these, 13 attended center P (32% of the center P cohort) and seven attended center S (11% of center S cohort), while no child was found to be a carrier in center A. All identified PRP serotypes at inclusion were 23F.

Among the 117 children not found to be carriers at the initial sampling stage, five were not sampled a second time and were excluded from the study. Acquisition of a PRP strain occurred in 28 of the remaining 112 children (25%). All resistant strains acquired during the study period were serotype 23F. The incidence rate was 1.45 per 1000 children days (95% CI: 0.87–2.03). The highest carriage rates of PRP were observed during the October to January period. The probability of acquiring a resistant strain was higher in centers where prevalence of resistant strains at inclusion was high (centers P and S versus center A; $p=0.063$, Figure 1). The nested case-control study for PRP acquisition shows that acquisition of a strain of PRP was correlated with prescription of antibiotics during the previous 3 months (odds ratio (OR)) 4.60; 95% CI: 1.15–19.48; $p=0.01$), prescription of amoxicillin (OR 3.75; 95% CI: 0.96–15.11; $p=0.02$) and exposure to tobacco smoke (OR 4.38; 95% CI: 1.10–18.14; $p=0.01$). No correlation was found between acquisition of a PRP strain and age group (≤18 months versus >18 months), sex, prior carriage of a penicillin-susceptible SP strain, presence of siblings, or possession of pets (Table 1).

The sample of children on which our survey was conducted was not a random but a convenience sample. However, the main object of this investigation was to observe trends in PRP carriage among children within a communal setting rather than to obtain prevalence rates for a given district. Our results suggest that horizontal transmission is the main factor responsible for nasopharyngeal colonization by PRP among children in communal settings. Acquired resistant strains were all serotype 23F. No occurrence of a switch from a susceptible to a resistant strain of the same serotype was noted, which is in favor of colonization rather than de novo mutation. Last, the probability of acquiring a resistant strain is correlated with the prevalence of that particular strain within the DCC. Moreover, the fact that the two hospital-based day-care centers were not similar regarding PRP carriage patterns while one of these was comparable to the private DCC does not suggest hospital staff as major vectors of resistant strains. The case-control study shows a correlation between carriage and prior antibiotic treatment, particularly with amoxicillin. Similar results have been reported in other studies [4,5]. Furthermore, a significant correlation appears with exposure to tobacco smoke, independently of antibiotic treatment; this is in favor of a specific effect of tobacco on bacterial colonization regardless of any infectious episode. Sung et al have reported that parental smoking was associated with higher carriage rates of SP without distinction of penicillin susceptibility, as appears also in this study [6]. However, no indication of its specific influence on carriage of resistant strains has apparently been noted up to now.

The emergence of penicillin-resistant strains of SP among the nasopharyngeal flora of young children raises the issue of its consequences in terms of morbidity and mortality resulting from infection due to such strains. Recent studies have confirmed the link between carriage rates and those responsible for invasive conditions [7,8]. On the basis of the results of this survey, it would seem appropriate to implement measures aimed at reducing carriage rates of resistant

**Table 1** Risk factors for acquiring PRP

| Risk factor | Cases ($n$=18) | Controls ($n$=36) | OR[1] | 95% CI[2] | $p$ |
|---|---|---|---|---|---|
| Exposure to tobacco smoke | 10 | 8 | 4.38 | 1.10–18.14 | 0.014 |
| Antibiotics | 13 | 13 | 4.60 | 1.15–19.48 | 0.012 |
| Amoxicillin | 10 | 9 | 3.75 | 0.96–15.11 | 0.02 |
| Prior carriage of susceptible SP | 12 | 30 | 0.40 | 0.09–1.80 | 0.16 |
| Pets | 4 | 12 | 0.57 | 0.12–2.49 | 0.40 |
| Siblings | 8 | 13 | 1.42 | 0.38–5.28 | 0.55 |

[1]OR=Odds Ratio [2]CI=Confidence interval.

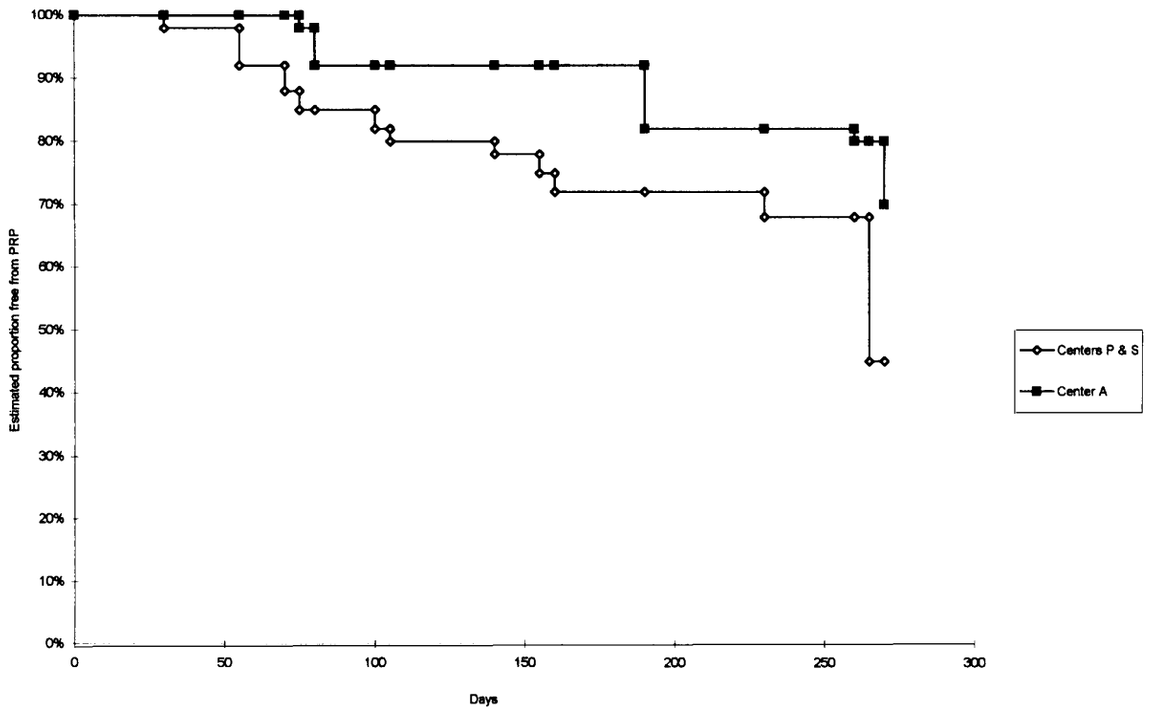


**Figure 1** Difference in probability of acquiring a PRP strain according to initial prevalence in day-care centers: center A versus centers P and S ($p$=0.063).

pneumococci in day-care centers, focusing on parents and medical practitioners in order to reduce certain risk factors (exposure to tobacco smoke, repeated treatment with amoxicillin).

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